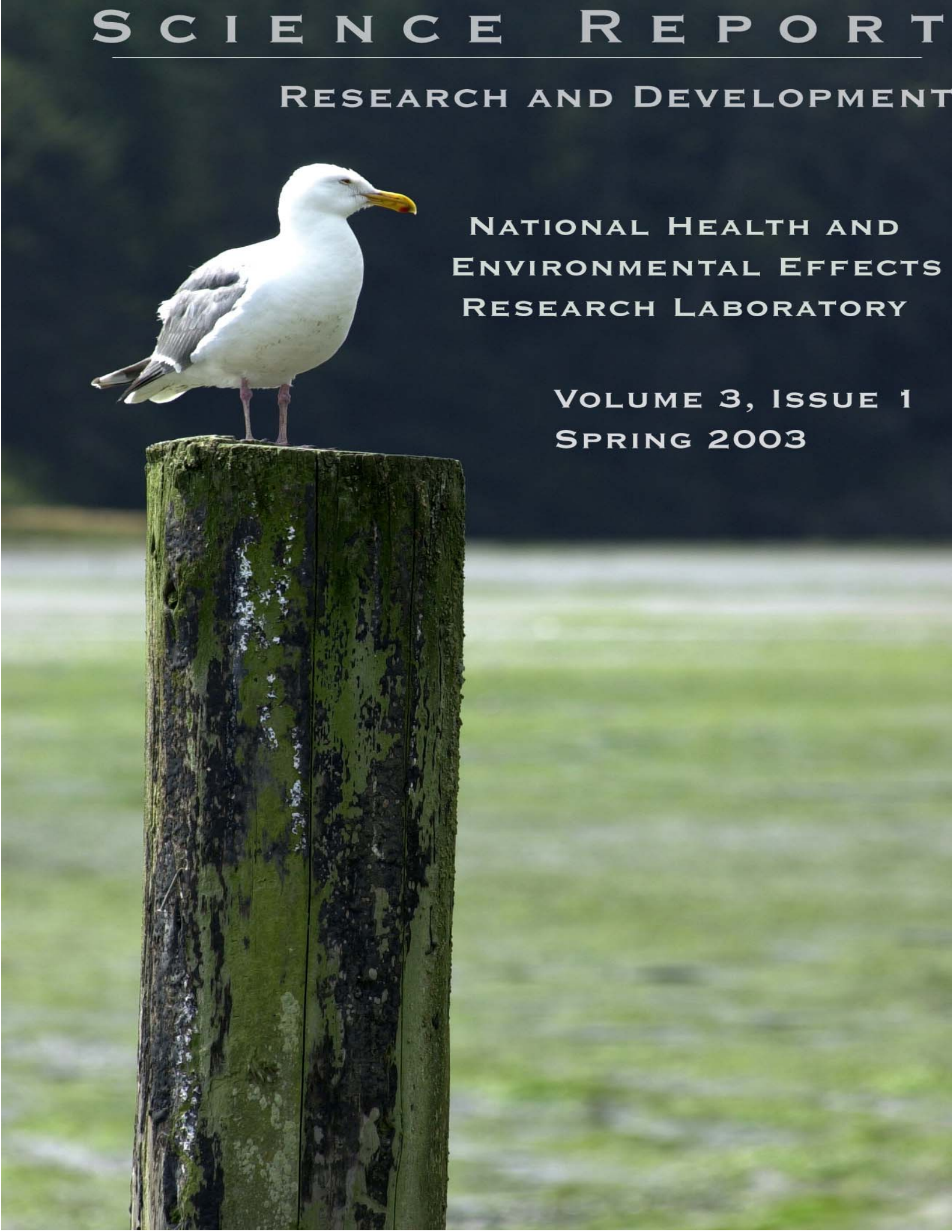
Science Report

Research and Development



National Health and Environmental Effects Research Laboratory

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RESEARCH

Particles from World Trade Center Collapse Cause Respiratory Toxicity in Mice

The September 11, 2001 terrorist attack on New York City's World Trade Center (WTC) caused an unprecedented environmental emergency. The collapse of the towers sent a tremendous cloud of crushed building materials and other pollutants into the air of lower Manhattan. Analysis of fallen dust samples collected in the first few days after the attack showed that 1 - 4% by weight consisted of particles small enough to be respirable. These particles included fine particulate matter, or $PM_{2.5}$ (PM less than 2.5 μm in diameter), which can be inhaled deep into the lungs and is associated with cardiovascular and respiratory health effects. Given the extremely high concentrations of dust immediately after the fall of the towers, even a relatively small proportion of $PM_{2.5}$ could have contributed to breathing problems in rescue workers and others who were not wearing protective masks.

In two papers recently accepted by *Environmental Health Perspectives* for publication in June 2003, scientists from the U.S. EPA, New York University, and Michigan State University examined the chemical properties of the $PM_{2.5}$ fraction of the dust derived from the destruction of the WTC and its toxicity in the respiratory tract of mice.

Samples of WTC $PM_{2.5}$ isolated from fallen dust collected 1 or 2 days after the disaster were composed of calcium-based compounds found in building materials. Assessment of short-term effects in mice 1 to 3 days after exposure showed that these samples caused mild to moderate degrees of lung inflammation when administered at a relatively high dose of 100 μg directly into the airways. The inflammation, however, was less than that caused by a toxic PM emission source (residual oil fly ash, ROFA) or a standard ambient air PM sample (NIST 1649a). Most importantly, this dose of WTC $PM_{2.5}$ caused airway hyper-responsiveness comparable to that from NIST 1649a and

greater than that from the toxic ROFA sample. The hyper-responsiveness indicates that the high dose group was primed to react to triggering agents that can constrict the airways. Lower doses of 10 and 32 μg administered directly into the airways, or the inhalation of 11 mg/m^3 in air (estimated to deposit approximately 14 μg of $PM_{2.5}$ in the respiratory tract), did not induce significant inflammation or hyper-responsiveness.

Although the concentrations of $PM_{2.5}$ immediately following the WTC collapse are unknown, it was estimated that healthy people exposed to about 425 μg/m^3 of WTC $PM_{2.5}$ in air for 8 hours would get a dose comparable to the high dose in the mice. The authors concluded that inhalation of high doses of WTC $PM_{2.5}$ derived from building materials could contribute to the development of pulmonary inflammation, airway hyper-responsiveness, and cough. Most people, however, would not be expected to experience adverse short-term respiratory effects from exposure to even moderately high WTC $PM_{2.5}$ levels (estimated at 130 μg/m^3 for 8 hours). The persistence of any effects of inhaled WTC $PM_{2.5}$ is unknown and was not addressed in these studies. These studies provide essential information on the chemistry and respiratory toxicity of WTC $PM_{2.5}$, which is a necessary component in the evaluation of health risks from the WTC disaster.

Although these research articles are not yet available in print, they are available online at *http://ehp.niehs.nih.gov/docs/admin/newest.html#11_17* . A full EPA report is available at *http://www.epa.gov/nheerl/wtc/WTC_report_7b3i.pdf* .

Exposure Risk Assessment Models Evaluated

In assessing human non-cancer risks from exposures to toxicants, EPA must judge which type of short-term acute exposure is most likely to lead to long-term, chronic, irreversible effects in the lungs. Five Experimental Toxicology Division scientists–Dr. Gary Hatch, Dr. Urmila Kodavanti, Dr. Dan Costa, Kay Crissman, and Ralph Slade–examined factors important in the progression from acute lung injury to

chronic formation of scar tissue (fibrosis). Rats were exposed to phosgene, a toxic industrial gas, under different conditions of time and exposure concentration, and both acute and chronic indicators of effect were measured. The results suggest that sharp peaks of exposure separated by long intervals induce more severe, chronic injury than continuous, low-level exposures.

Traditionally, EPA has judged the potential for chronic effects of air pollutants by using a mathematical calculation of exposure dose. The pollutant concentration is multiplied by the time of exposure to estimate the total dose of the toxic agent. This "concentration-time model" makes long-term, low-concentration exposures appear the same as short-term, high-concentration exposures, but it appears that the model may underestimate effects that occur during episodic exposures to phosgene and other air toxics with similar reactivity. Persistent lung injury to rodents was highest after a series of intermittent spikes of exposure. Longer times between exposure appeared to allow adaptation to disappear, causing greater injury with each subsequent exposure spike and, ultimately, greater chronic injury. A conceptual model was developed to relate acute injury, adaptation, and chronic lung injury. [*Toxicology and Industrial Health*, 17(Issue 5-10):285-293].

Reactive Oxygen Species Implicated in DNA Damage Caused by Arsenicals

Recent research in the Environmental Carcinogenesis Division (ECD) further explains the mode of action of two genotoxic arsenic compounds. The genotoxic effect of arsenic arises from reactive oxygen species (ROS) generated from two methylated trivalent forms of inorganic arsenic, MMA^{III} and DMA^{III}. These findings may eventually lead to revision of the extrapolation model currently used to estimate human cancer risk from arsenic exposure.

In 2001 EPA proposed a lower Maximum Contaminant Level (MCL) of 10 µg/L for arsenic, based on published research on arsenic-exposed populations in Taiwan, China,

but without knowing the actual mode of action for arsenic. Given the new information from ECD, the shape of the arsenic dose-response curve may differ from that used in the original model.

Naturally occurring inorganic arsenic exists in drinking water in two major forms: arsenite and arsenate. In mammals, inorganic arsenic is biotransformed by methylation into a number of organometallic forms of arsenic, which have been found in the urine of humans and rodents exposed to arsenic in their drinking water. Two of these forms are MMA^{III} and DMA^{III}, both of which had been previously shown by NHEERL researchers to damage the DNA of mammalian cells in culture. The current research uncovered the genotoxic mode of action of these arsenicals.

ROS are identified as arsenic-derived intermediates in the DNA damage process. Research by Dr. Stephen Nesnow, the late Dr. Marc Mass, Barbara Roop, and Guy Lambert (all of ECD), with colleagues from the National Institute of Environmental Health Sciences and the University of British Columbia, found that four ROS inhibitors, including the hormone melatonin and an antioxidant analog of Vitamin E, were extremely effective in preventing the DNA-damaging effects of both arsenicals.

The researchers used a special spectroscopic technique to identify the hydroxyl radical as the ROS form responsible for the DNA damage. The ROS are generated during the process of air oxidation of the trivalent arsenicals to their pentavalent forms. The ECD researchers concluded that methylated trivalent forms of consumed inorganic arsenic damage DNA through the formation of ROS. [*Chemical Research in Toxicology*, 2002, 15:1627-1634].

Confocal Microscopy Gives Enhanced 3-D Images of Biological Structures

Confocal microscopy, an important technique used to visualize biological structures in three dimensions, is the foundation of many toxicological assays. A recent

paper by Dr. Robert Zucker of the Reproductive Toxicology Division evaluates the performance of the confocal laser-scanning microscope (CLSM) used in a wide variety of projects, including the effects of methoxychlor on rat pituitary and ovary, atrazine on rat prostate development, and ethanol administration to pregnant mice on the development of areas of the brain in the offspring.

CLSM data consists of digital images that are similar to photographs, and these images can be obtained even if the equipment is performing sub-optimally. CLSM data are most reliable, however, when the instrument is correctly aligned and the laser power is stable. This paper describes the equipment needed for performance testing, which includes a photomultiplier detector to measure fluorescent light emission, a custom-made detector holder built in the NHEERL machine shop to fit onto the microscope, and an inexpensive, portable power meter to measure the amount of emitted light. A power output test can determine whether the system is misaligned, functioning badly, or if the laser needs to be replaced. The paper includes a reference table that compares maximum power output using different types of equipment and lasers. The table will be especially valuable in assessing the performance of CLSM systems used in other laboratories. This new technique for optimizing confocal microscope performance is now available to the broader scientific research community. It will improve the accuracy and reliability of data collected, which are important factors for data gathered for regulatory decision making. [*Microscopy Today*, 2002, 10(6):20-22].

Model Forecasts Atrazine and PCB Concentrations in Lake Michigan

To assist managers in remedial and regulatory decision-making, a multimedia mathematical modeling framework was applied to Lake Michigan, the sixth largest lake in the world. The Mid-Continent Ecology Division (MED), cooperating with EPA Region 5; the EPA Great Lakes National Program Office; the states of Michigan, Wisconsin, Illinois, and Indiana; the First Nations (Native American tribes); and other federal, public, and private groups, completed the 2002 Lake Michigan Lakewide Management Plan (LaMP).

MED used mass balances of atrazine and PCBs to predict several concentrations of these pollutants under different remedial or regulatory scenarios for setting priorities with lakewide and local watershed perspectives. The LaMP for each of the five Great Lakes is updated every two years. It summarizes the current status of the lake, tracks significant activities and new initiatives, and describes improvements in habitat, cleanup, indicators, and contaminants.

The mass balance shows that approximately 70% of the atrazine loading is from tributaries and 30% from atmospheric wet deposition. The greatest tributary loads originate from the St. Joseph, Grand, and Fox Rivers. Forecasts indicate that atrazine concentrations will increase from 40 to 70 ng/L over the next 150-200 years at present loadings. A 57% reduction in tributary loading would be required to maintain the 40 ng/L concentration under the "no further degradation" clause of the U.S./Canada Water Quality Agreement and the Clean Water Act. Present and forecasted lakewide atrazine concentrations fall below U.S. EPA thresholds for fish (20,000 ng/L), invertebrates (10,000 ng/L), non-vascular plants (2,300 ng/L), and vascular plants (2,300 ng/L) in freshwater lakes and reservoirs. Additional information is available at the following Web site: http://www.epa.gov/oppsrrd1/reregistration/atrazine .

In contrast, PCB concentrations in Lake Michigan are dominated first by dynamic interactions and processes of sediments with the water column, then by substantial inputs from the atmosphere, and finally by contributions from tributaries. The largest tributary contributors are the Fox, Grand Calumet, and Kalamazoo Rivers. Model forecasts indicate that even with no further remedial action, PCB concentrations in lake trout will continue to decrease, but that the rate of decrease could be accelerated by further reductions in atmospheric deposition and tributary inputs. As PCBs are depleted from sediments by resuspension from sediments to water, volatilization into the atmosphere, and losses to deep burial in sediments, the PCB atmospheric vapor concentration (global background) will drive the system. Forecasts indicate that a 50% reduction in atmospheric and tributary loads would further decrease PCB concentrations

in lake trout and move closer to achieving the target level of 0.05 ppm for the unlimited consumption of fish by humans. See the following Web site for additional information: http://www.michigan.gov/mesb/0,1607,7-117-1254-28636-,00.html .

The 100-page LaMP for Lake Michigan is available at the following Web site: http://www.epa.gov/glnpo/lakemich/lm02/index.html .

PUBLICATIONS

Accounting for Organic Carbon Held in Forest Soils in the U.S. and Puerto Rico

Because of intense concern that increasing levels of atmospheric carbon dioxide may be causing global climate change, identifying ecosystems that can sequester and store carbon is a high priority. Scientists in the Western Ecology Division (WED) have completed an inventory of the organic carbon currently held in forest soils in the United States and Puerto Rico. Organic carbon in soils is derived from the photosynthetic fixation of atmospheric carbon dioxide that enters the soil through plant roots or plant litter (leaves, branches, etc.) deposited in or on the soil surface. Soils are the largest terrestrial reservoir of carbon (approximately three times that held in global vegetation and twice that held in the atmosphere).

In Chapter 4 of *The Potential of U.S. Forest Soils to Sequester Carbon and Mitigate the Greenhouse Effect*, a book edited by J.M. Kimble et al. and published by CRC Press in 2002, Dr. Mark G. Johnson of WED and Jeffrey Kern of Dynamac Corporation use the inventory as a baseline for monitoring future changes in the amount of soil carbon held in forested systems and for identifying those forest types that may be managed to sequester additional carbon below ground.

To create a map of soil carbon for the contiguous U.S. and Puerto Rico, the researchers determined spatial patterns and total soil organic carbon in forests by using digital soil survey data linked to a large national soil-characterization database. They then combined the resultant soil organic carbon maps with existing maps of forest types to create new maps showing the geographical distribution of carbon in forest soils. Tables list the amounts of soil organic carbon at three depths in various types of forests and distinguish between the contribution of organic soils and mineral soils to total soil carbon. In forested areas of the United States and Puerto Rico, Johnson and Kern

estimate that the amount of carbon held in the upper 100 centimeters of soil to be 35.5 petagrams of carbon (one petagram is equal to 10^{15} grams or 1000 million metric tons).

Proceedings for "Coastal Monitoring Through Partnerships" Published

The proceedings for EMAP 2001, "Coastal Monitoring Through Partnerships," a symposium of the EPA Environmental Monitoring and Assessment Program (EMAP) held in Pensacola, Florida, have been published recently in both journal and book format. The publications contain 33 peer-reviewed papers describing multidisciplinary coastal and estuarine environmental monitoring programs designed and implemented by EPA in partnership with federal and state agencies, academia, Native American tribes, and non-governmental organizations. The international journal, *Environmental Monitoring and Assessment*, devoted the entire January 2003 special issue (Volume 81, Issue1-3) to the proceedings. Journal subscribers can access the full papers online at the following URL: http://www.kluweronline.com/issn/0167-6369 . Non-subscribers have free access to the abstracts at the same URL. A hard-cover book version (ISBN 1-4020-1089-3, 420 pages), is also available.

Throughout, the papers emphasize how successful partnerships were used to identify, diagnose, and solve coastal environmental problems and how research and technology transfer have led to more efficient, less expensive, and more scientifically rigorous monitoring and assessment programs.

Three NHEERL scientists (Dr. Brian Melzian of the Atlantic Ecology Division, Virginia Engle of the Gulf Ecology Division, and Dr. Shabeg Sandhu of EMAP) and Malissa McAlister of the Council of State Governments served as scientific editors.

AWARDS

GED Scientist Honored with SETAC Government Service Award

Dr. Foster "Sonny" Mayer of the Gulf Ecology Division (GED) received the 2002 Society of Environmental Toxicology and Chemistry Government Service Award at the society's annual meeting in Salt Lake City, Utah, November 16-20, 2002. The award recognizes exemplary dedication and service in promoting the application of environmental toxicology and chemistry to risk assessment in a government function; fostering programs that aid in the development of ecologically sound and acceptable practices and principles; and providing a forum for communication. Dr. Mayer was recognized for service in all three areas during his long career, first with the U.S. Fish and Wildlife Service (1970-84) and then with EPA (1985-present).

Dr. Mayer's contributions have ranged from the first two workshops on ecological risk assessment in the late 1970s to his recent development of probability-based risk assessment techniques used in evaluating national water quality criteria for the protection of endangered species. Other career highlights include serving as U.S. Science Advisor in the US-USSR Scientific Exchange; promoting multidisciplinary research in toxicology and risk assessment on a watershed basis; helping create of SETAC in 1979; and publishing 126 journal articles, reports, books, and book chapters. He also had appointments at five universities, where he was research advisor or committee member for 16 master's and 10 doctoral candidates.

SETAC membership is drawn from government, universities, business, and public-interest groups from more than 70 countries. More than 5,000 individual members have technical specialities in chemistry, toxicology, ecology, atmospheric health, earth sciences, and environmental engineering; and Dr. Mayer's eclectic background overlapped many of them.